CLAIMS

1. Process for preparing cephradine, said process comprising reacting 7-aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form (DHa) in the presence of an enzyme in a reaction mixture to form cephradine, resulting in a conversion of 7-ADCA into cephradine of at least 70 %, wherein the concentration D-dihydrophenylglycine (DH) in the reaction mixture is below 2 wt.%.

2. Process according to claim 1, wherein said reacting results in a conversion of 7-ADCA into cephradine of at least 80%, preferably at least 90%.

3. Process according to claim 1 or 2, wherein said reacting results in a conversion of D-dihydrophenylglycine in activated form (DHa) into cephradine (CEF) of at least 70%, preferably at least 80%, more preferably at least 90%, wherein

the conversion of DHa into CEF = $(n_{CEF} / n_{DHa})*100\%$;

n_{CEF} = quantity of cephradine formed (in mole); and

n_{DHa} = total quantity of DHa added to reaction mixture (in mole).

4. Process according to any one of the claims 1 to 3, wherein the concentration DH in the reaction mixture is maintained below 2 wt.%, preferably below 1 wt.% throughout said reacting by controlling the pH of the reaction mixture and/or the temperature.

5. Process according to any one of the claims 1 to 4, wherein the sum of the quantity of 7-ADCA added to the reaction mixture and DHa added to the reaction mixture is between 10 and 2000 mmol per liter of reaction mixture, preferably between 50 and 1500 mmole per liter of reaction mixture.

6. Process according to any one of the claims 1 to 5, characterised in that dihydrophenylglycine in activated form is dihydrophenylglycine methylester.

7. Process according to any one of the claims 1 to 6, characterised in that dihydrophenylglycine in activated form is a HCl salt of dihydrophenylglycine methylester.

8. Process according to any one of the claims 1 to 7, characterised in that said reacting is carried out at a temperature between –5 and 35 °C.

9. Process according to any one of the claims 1 to 8, characterised in that said reacting is carried out at a pH of between 6 and 9.

10. Process according to any one of the claims 1 to 9, characterised in that said enzyme is a penicillin acylase.

11. Process according to any one of the claims 1 to 10, characterised in that the enzyme is immobilised on a carrier.

12. Process according to any one of the claims 1 to 11, wherein the process is a batch process.

13. Process according to any one of the claims 1 to 12, characterised in that said enzyme is an acylase having a higher S/H ratio than the wild-type acylase of *E.coli*.

14. Process for preparing cephradine, preferably according to any one of claims 1 to 12, said process comprising reacting 7-ADCA with DHa in the presence of an enzyme in a reaction mixture to form cephradine, wherein said enzyme is a wild type penicillin acylase, and wherein said reacting is carried out at a temperature below 15 °C.

15. Process according to claim 14, wherein said reacting is carried out at a pH of at least 7.0.

16. Process for preparing cephradine, preferably according to any one of the claims 1 to 13, said process comprising reacting 7-ADCA with DHa in the presence of an enzyme in a reaction mixture to form cephradine, wherein said enzyme is an acylase having a higher S/H ratio than the wild-type acylase of *E.coli*, and wherein said reacting is carried out at a temperature of at least 15 °C.

17. Process according to claim 16, wherein said reacting is carried out at a pH of below 7.7.

18. Process according to claim 16 or 17, characterised in that the enzyme is a mutant penicillin acylase.

19. Process according to any one of the claims 1 to 18, wherein the process comprises crystallising the cephradine from an aqueous solution.

20. Process, preferably according to claim 19, said process comprising:

reacting aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form (DHa) in the presence of an enzyme in a reaction mixture to form cephradine; and

crystallising the cephradine from an aqueous solution, in which aqueous solution the ratio $m_{CEF}/(m_{7\text{-}ADCA} + m_{CEF}) > 0.7$, preferably > 0.8, more preferably > 0.9, and wherein x_{DH} = 0-2 wt.%, preferably 0-1 wt.%, wherein

m_{CEF} = molar quantity of cephradine in the aqueous solution;

$m_{7\text{-}ADCA}$ = molar quantity of 7-ADCA in the aqueous solution; and

x_{DH} = concentration of DH in the aqueous solution relative to the total weight of the aqueous solution.

21. Process according to claim 19 or claim 20, wherein the process comprises separating the enzyme from the cephradine prior to said crystallising.

22. Process according to any one of the claims 1 to 21, wherein the concentration 7-ADCA in the aqueous solution is between 0 and 5 wt.%, preferably between 0 and 2 wt.%.

23. Process according to any one of the claims 19 to 22, wherein said crystallising is performed at a temperature of between 45 and 60 °C, preferably between 48 and 55 °C.

24. Process for preparing cephradine hydrate crystals, characterised in that the process comprises crystallising cephradine from an aqueous solution to form

cephradine hydrate, wherein said crystallising is carried out at a temperature of between 45 and 60°C, preferably between 48 and 55°C.

25. Process according to any one of claims 19 to 24, wherein said crystallising is performed at a pH of between 4.0 and 6.0, preferably at a pH of between 4.5 and 5.5.

26. Process for the preparation of cephradine characterised in that the process comprises:

- reacting 7-aminodesacetoxy cephalosporanic acid (7-ADCA) with D-dihydrophenylglycine in activated form in the presence of an enzyme in a reaction mixture to prepare cephradine; and
- crystallising the cephradine from an aqueous solution to form cephradine hydrate according to the process according to claim 24 or 25.

27. Process according to any one of the claims 1 to 23 or claim 26, wherein part of the cephradine formed is present in the reaction mixture as cephradine hydrate, and wherein the process comprises dissolving at least part of said cephradine hydrate.

28. Process according to claim 27, wherein said dissolving is effected at a pH of above 8, preferably at a pH of between 8.5 and 9.

29. Process according to any one of the claims 19 to 28, characterised in that said crystallising is performed at such pH and at such temperature that the absorbance at 450 nm of the cephradine hydrate prepared is below 0.050.

30. Process according to any one of the claims 1 to 23 characterised in that said reacting is carried out in the presence of sodium bisulphite.

31. Cephradine hydrate obtainable by the process according to any one of the claims 1 to 30.

32. Cephradine hydrate with an absorbance at 450 nm of less than 0.050.